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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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MICHAEL BEST & FRIEDRICH, LLP ONE SOUTH PINCKNEY STREET P O BOX 1806 MADISON, WI 53701			STEADMAN, DAVID J	
			ART UNIT	PAPER NUMBER
			1656	

DATE MAILED: 05/31/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/016,403	HOLLADAY, LESLIE A.	
	Examiner	Art Unit	
	David J. Steadman	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 January 2006 and 31 January 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,4-24 and 26-28 is/are pending in the application.
- 4a) Of the above claim(s) 5-16 and 19-24 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,4,17,18,26 and 28 is/are rejected.
- 7) ☒ Claim(s) 27 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of the Application

- [1] Claims 1, 4-24, and 26-28 are pending in the application.
- [2] Applicant's amendment to the claims, filed on 1/13/2006, is acknowledged. This listing of the claims replaces all prior versions and listings of the claims. It is noted that the status identifiers for claims 2-3 and 25 is not in a parenthetical expression as required by 37 CFR 1.121. See MPEP 714, which states (in relevant part), "[a]fter each claim number, the status identifier of the claim must be presented in a parenthetical expression."
- [3] Receipt of a terminal disclaimer, filed on 1/13/2006, is acknowledged.
- [4] Applicant's arguments filed on 1/13/2006 have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.
- [5] The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.

Election/Restriction

- [6] Claims 5-16 and 19-24 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the replies filed on 3/29/2004 and 1/31/2005.

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[7] Claims 1, 4, 17-18, and 26-28 are being examined on the merits.

Claim Rejections - 35 USC § 112, First Paragraph

[8] The scope of enablement rejection of claims 1, 4, and 17-18 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record and the reasons stated below. The rejection was fully explained in a prior Office action.

RESPONSE TO ARGUMENT: Applicant argues the specification combined with the knowledge of the skilled artisan is sufficient to enable one of skill in the art to make and use the full scope of the claimed invention. Applicant specifically argues 1) peptide synthesis methods were conventional at the time of the invention; 2) histidine modified peptides provide increased electrophoretic mobility due to increased hydrophilicity and a higher net positive charge; 3) a Thr to His substitution is a conservative substitution, thus preserving the hydrophobicity, net physiological pH, side chain volume, and hydrogen bonding ability of the parent polypeptide; 4) the specification discloses working examples of the claimed method.

Applicant's argument is not found persuasive. While the prior art reference of Märki et al. (*Hoppe-Seyler's Z. Physiol Chem* 360:1619-1632, 1979) recognizes at least one working example of a synthetic analog of a pharmaceutical polypeptide having a Thr to His mutation, the claims broadly encompass a method using *any* synthetic analog of a pharmaceutical polypeptide having *any* Thr residue replaced with His. The effects of altering the amino acid sequence of a polypeptide on its function, even a single amino acid alteration, are highly unpredictable (see "Introduction to Protein Structure,"

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Branden and Tooze, Garland Publishing, Inc., New York, 1991, p. 247), which is undisputed by applicant. The high level of unpredictability is further evidenced by the references of Colman (*Res Immun* 145:33-36) and Abaza et al. (*J Prot Chem* 11:433-444), which teach that single amino acid changes within the interface of an antigen-antibody complex or even outside of an antigenic site can abolish the interaction entirely (p. 33, bottom of Colman and p. 433, abstract, of Abaza et al.). That substitution of Thr with His can have unexpected and negative effects on a protein's activity are evidenced by Obermuller et al. (*J Cell Sci* 115:185-194, 2002), which discloses that a Thr to His substitution in a Lamp 1 polypeptide *significantly* reduces the protein-protein interaction between Lamp 1 and AP1 (p. 190, right column, bottom). The disclosure of the specification, which includes generalized teachings regarding substitution of Thr with His, fails to remedy the highly unpredictable nature of amino acid alteration on the function of a polypeptide. It should be noted that the specification fails to disclose even a single working example of the claimed method. As such, a skilled artisan must experiment without the necessary guidance provided by the specification or prior art to determine which analogs would retain the biological activity of the parent polypeptide such that the analogs would have the desired therapeutic effect. In view of the breadth of the claims, the lack of guidance and working examples, the high level of unpredictability and the amount of experimentation involved, it is the examiner's position that undue experimentation is required for a skilled artisan to make and use the full scope of the claimed invention.

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[9] Claim 28 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. Claim 28 is drawn to the method of claim 1, wherein the parent polypeptide is human growth hormone releasing hormone. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is the examiner's position that undue experimentation would be required for a skilled artisan to make and/or use the claimed invention. Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)) as follows: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. See MPEP § 2164.01(a). The Factors most relevant to the instant rejection are addressed in detail below.

The breadth of the claim: Claim 28 is drawn to a method for delivering a synthetic analog of h-GHRH, wherein the synthetic analog of h-GHRH has a Thr replaced with His, by delivering the synthetic analog through a body surface by electrotransport. The breadth of the claim is narrow. The specification specifically defines h-GHRH as "a 44 amino acid polypeptide containing glutamine residues at positions 16, 24, 30, 31 and 36

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(SEQ ID NO:8)" (p. 13, lines 20-22). The sequence of SEQ ID NO:8 has only a single Thr residue at position 7 of SEQ ID NO:8.

The state of the prior art; The level of one of ordinary skill; and The level of predictability

in the art: As noted above, the effects of altering the amino acid sequence of a polypeptide on its function, even a single amino acid alteration, were highly unpredictable at the time of the invention (see "Introduction to Protein Structure," Branden and Tooze, Garland Publishing, Inc., New York, 1991, p. 247). The high level of unpredictability is further evidenced by the references of Colman (*Res Immun* 145:33-36) and Abaza et al. (*J Prot Chem* 11:433-444), which teach that single amino acid changes within the interface of an antigen-antibody complex or even outside of an antigenic site can abolish the interaction entirely (p. 33, bottom of Colman and p. 433, abstract, of Abaza et al.). The specification discloses that a Gln to His mutation in a polypeptide is considered to be even more conservative than a Thr to His mutation. However, even a Gln to His substitution can disrupt protein-protein interaction as acknowledged by the reference of Colman, which teaches that Gln to His mutation in lysozyme disrupts binding to an anti-lysozyme antibody (p. 34, left column, bottom). If a Gln to His mutation, which is disclosed as being more conservative than a Thr to His mutation, can disrupt protein-protein interaction, then it follows that a Thr to His substitution can also have such an effect. That substitution of Thr with His can have unexpected and negative effects on a protein's activity is also evidenced by Obermuller et al. (*J Cell Sci* 115:185-194, 2002), which discloses that a Thr to His substitution in a Lamp 1 polypeptide *significantly* reduces the protein-protein interaction between Lamp 1

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and AP1 (p. 190, right column, bottom). In view of the cited teachings, a skilled artisan would have recognized that, at the time of the invention, one could not predict the resulting functional effect(s) of replacing Thr with His in a polypeptide. “[I]f one skilled in the art cannot readily anticipate the effect of a change within the subject matter to which that claimed invention pertains, then there is lack of predictability in the art.” See MPEP § 2164.03.

The amount of direction provided by the inventor and The existence of working

examples: While the specification at pp. 10-12 discloses general, nonspecific guidance for altering the amino acid sequence of a protein, the specification fails to disclose even a single working example of the claimed invention. While MPEP § 2164.02 states, “[c]ompliance with the enablement requirement of 35 U.S.C. 112, first paragraph, does not turn on whether an example is disclosed,” it acknowledges that “[l]ack of a working example, however, is a factor to be considered, especially in a case involving an unpredictable and undeveloped art.” Because of the high level of unpredictability associated with amino acid substitution, a skilled artisan would have no reasonable expectation that replacing Thr in SEQ ID NO:8 with His would result in a polypeptide having the desired biological activity.

In view of the lack of guidance and working examples provided in the specification and the high level of unpredictability as evidenced by the prior art, undue experimentation would be necessary for a skilled artisan to make and use the entire scope of the claimed invention. Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those

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skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 103

[10] The rejection of claims 1, 4, and 17-18 under 35 U.S.C. 103(a) as being unpatentable over Chien et al. in view of Green et al. and Markussen et al. is withdrawn in view of applicant's amendment to claim 1 to limit the synthetic analog to having a threonine to histidine substitution. The combined references of Chien et al., Green et al., and Markussen et al. fail to teach or suggest a synthetic analog polypeptide having a Thr to His substitution.

[11] Claims 1, 4, and 17-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chien et al. (*J Pharm Sci* 78:376-383, 1989; cited in the IDS filed on 2/28/2002) in view of Sage et al. (US Patent 5,494,679; cited in the IDS filed on 2/28/2002), Märki et al. (*Hoppe-Seyler's Z. Physiol Chem* 360:1619-1632, 1979), Green et al. (*Pharmaceutical Res* 8:1121-1127, 1991; cited in the IDS filed on 2/28/2002), and Voet et al. ("Biochemistry," John Wiley and Sons, New York, 1990). Claim 1 is drawn to a method for delivering synthetic analog of a parent pharmaceutical polypeptide, wherein the synthetic analog has a Thr replaced with His, by delivering the synthetic analog through a body surface by electrotransport. Claim 4 requires that the analog have about the same type and amount of biological activity as the parent polypeptide. Claims 17-18 limit the pH of the anionic donor reservoir formulation.

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The reference of Chien et al. teaches methods for the administration of insulin by iontophoresis (see particularly pp. 378-380) using a donor solution at pH 3.7, 5.2, or 7.1 (p. 380, Table III). The reference of Chien et al. does not teach iontophoretic delivery of an insulin analog having a Thr replaced with His.

The reference of Märki et al. teaches the synthesis and biological activity of human insulin analogs, in particular an analog wherein Thr at position 8 of the A chain (A8) is replaced with His (p. 1622, Table 1). Märki et al. teaches that the A8 His analog has an increased isoelectric point relative to unmodified human insulin (p. 1622, Table 1) and that this analog was the only analog that exhibited a potency greater than unmodified human insulin (p. 1629, right column and p. 1631, left column, bottom).

The reference of Sage et al. teaches a method for iontophoretic delivery of insulin through skin (see particularly Examples 2-3). Sage et al. teaches iontophoretic delivery of a therapeutic peptide can be improved by, *inter alia*, using an analog of a peptide, wherein the analog has an altered isoelectric point outside the range of skin (column 3, lines 57-60) and using a peptide having high water solubility (column 4, lines 7-13). With respect to altering the isoelectric point outside the range of skin, the reference of Sage et al. teaches the isoelectric point of a bioactive peptide can be modified by replacing a neutral amino acid residue with a positively charged residue (column 5, lines 23-25), which has the added effect of improving water solubility (column 5, lines 53-57). Sage et al. teaches that while the modification to enhance iontophoretic delivery "may lead to some loss of activity, as long as the intended result is achieved, loss of some bioactivity is acceptable" (column 4, lines 21-25).

As noted above, the reference of Sage et al. teaches replacing a neutral amino acid residue with a positively charged residue. Although the reference Sage et al. does not specifically suggest replacing a neutral amino acid with *His*, motivation to practice iontophoresis using a peptide with a neutral amino acid replaced with His is provided by the reference of Green et al., which teaches iontophoresis of Ala-X-Ala tripeptides where X was a neutral, negative, or positive (His) amino acid. Green teaches that the iontophoretic enhancement of the Ala-His-Ala was greater than peptides with neutral amino acids at the X position (p. 1124, left column; p. 1126, right column; and comparison of Figure 5(a) to Figures 1, 3, 6, and 7).

Furthermore, although the references of Chien et al., Sage et al., and Märki et al. do not specifically disclose Thr as a neutral amino acid and His as a basic amino acid, Voet et al. evidences this by teaching that the side chain of threonine is uncharged (p. 63, right column, bottom), while the side chain of histidine is positively charged at physiological pH (p. 64, left column, middle).

Therefore, at the time of the invention it would have been obvious to one of ordinary skill in the art to combine the teachings of Chien et al., Sage et al., and Märki et al. to practice the method of iontophoretic delivery of a insulin according to Chien et al. using the A8 His insulin analog of Märki et al. One would have been motivated to use the A8 His insulin analog of Märki et al. in practicing the method of Chien et al. because the A8 His insulin analog of Märki et al. has an increased isoelectric point as suggested by Sage et al. and additionally has the advantage of having greater potency as compared to the corresponding unmodified human insulin. One would have been further

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motivated to use the peptide of Märki et al. because of the teachings of Green et al. that iontophoretic enhancement of Ala-His-Ala with a positively charged His was greater than peptides with a neutral amino acid. One would have had a reasonable expectation of success for practicing the method of iontophoretic delivery of the peptide of Märki et al. according to the method of Chien et al. because of the teachings of Chien et al. and Märki et al. Therefore, claims 1, 4, and 17-18, drawn to the method described above would have been obvious to one of ordinary skill in the art at the time of the invention.

[12] Claim 26 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kumar et al. (*Proc Intern Symp Control Rel Bioact Mater* 17:435-436, Controlled Release Society, Inc., 1990) in view of Sage et al. (US Patent 5,494,679; cited in the IDS filed on 2/28/2002), Vale et al. (US Patent 4,528,190), and Voet et al. ("Biochemistry," John Wiley and Sons, New York, 1990). Claim 26 is drawn to a method for delivering a pharmaceutical polypeptide agent through a body surface by providing a synthetic analog of human growth releasing hormone (h-GHRH) having at least one Gln to His substitution and delivering the analog through the body surface by electrotransport.

The reference of Kumar et al. teaches a method of iontophoretic delivery of h-GHRH (referred to as growth releasing factor or GRF in the references of Kumar et al., Sage et al., and Vale et al.) in a hairless guinea pig. Kumar et al. teaches h-GHRH was delivered in a buffer at pH 5.8 (p. 435, left column, bottom). The reference of Kumar et al. does not teach iontophoretic delivery of a h-GHRH analog having a Gln replaced with His.

Sage et al. teaches that iontophoretic delivery of a therapeutic peptide can be improved by the following: (1) using an analog of a peptide, wherein the analog has an altered isoelectric point outside the range of skin (column 3, lines 57-60), wherein the isoelectric point is modified by replacing a neutral amino acid with a positively charged amino acid (column 5, lines 23-25); (2) using a peptide having high water solubility (column 4, lines 7-13), wherein water solubility is enhanced by replacing a neutral amino acid with a positively charged amino acid (column 5, lines 53-57); and (3) using a peptide of minimal size that maintains biological activity (column 3, lines 61-62), specifically teaching that h-GHRH can be reduced from its native 44 amino acid size by deleting C-terminal residues and still maintain "high potency" (column 5, lines 3-16).

As noted above, the reference of Sage et al. teaches replacing a neutral amino acid residue with a positively charged residue. Although the reference Sage et al. does not specifically suggest replacing a neutral amino acid with *His*, motivation to practice iontophoresis using a peptide with a neutral amino acid replaced with His is provided by the reference of Green et al., which teaches iontophoresis of Ala-X-Ala tripeptides where X is a neutral, negative, or positive (His) amino acid (p. 1121, abstract, top). Green et al. teaches that the iontophoretic enhancement of the Ala-His-Ala was greater than peptides with neutral amino acids at the X position (p. 1124, left column; p. 1126, right column; and comparison of Figure 5(a) to Figures 1, 3, 6, and 7).

The reference of Vale et al. teaches synthetic peptide analogs of h-GHRH, including a specific peptide analog (Example XXVI) of h-GHRH that has a smaller size as compared to native human growth hormone releasing factor due to deletion of C-

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terminal residues and has a mutation to replace Gln at position 24 of h-GHRH with His (column 12). Vale et al. teaches the Example XXVI peptide is considered to be biologically active (column 15, lines 48-49), useful for therapeutic applications in humans (column 16, lines 36-39), and has “generally greater” potency than a corresponding unmodified h-GHRH peptide (column 15, lines 44-48).

Although the references of Kumar et al., Sage et al. and Vale et al. do not specifically disclose Gln as a neutral amino acid and His as a basic amino acid, Voet et al. evidences this by teaching that the side chain of glutamine is uncharged (p. 63, right column, bottom) and the side chain of histidine is positively charged at physiological pH (p. 64, left column, middle).

Therefore, at the time of the invention it would have been obvious to one of ordinary skill in the art to combine the teachings of Kumar et al., Sage et al. and Vale et al. to practice the method of iontophoretic delivery of h-GHRH according to Kumar et al. using the Example XXVI peptide of Vale et al. One would have been motivated to use the Example XXVI peptide of Vale et al. in the method of Kumar et al. because the Example XXVI peptide of Vale et al. has all of the improvements suggested by Sage et al. in that it has a reduced size relative to native h-GHRH and has a neutral amino acid at position 24 – Gln – replaced with a positive amino acid – His – and additionally has the advantage of having greater potency as compared to a corresponding unmodified h-GHRH. One would have been further motivated to use the Example XXVI peptide of Vale et al. because of the teachings of Green et al. that iontophoretic enhancement of an Ala-His-Ala peptide was greater than peptides with a neutral amino acid. One would

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have had a reasonable expectation of success for practicing the method of iontophoretic delivery of h-GHRH according to Kumar et al. using the Example XXVI peptide of Vale et al. because of the teachings of Kumar et al. and Vale et al. Therefore, claim 26, drawn to the method described above would have been obvious to one of ordinary skill in the art at the time of the invention.

Examiner Comment/Clarification

[13] In the prior Office action, the examiner noted that “the specification discloses ‘[h]uman growth hormone releasing hormone (h-GHRH) is a 44 amino acid polypeptide containing glutamine residues at positions 16, 24, 30, 31 and 36 (SEQ ID NO:8) (p. 13, lines 20-22)’” and that “[i]n this way, the specification specifically defines ‘human growth releasing hormone’ polypeptide as being the polypeptide of SEQ ID NO:8.” In response to the examiner’s remarks, applicant asserts that “[w]hile the specification makes clear that SEQ ID NO:8 is clearly an example of ‘human growth hormone releasing hormone,’ the specification also indicates that such a sequence is merely an illustrated example of an analog of ‘human growth releasing hormone’” (referring to the disclosure at p. 12, ll. 28-31) and that “[o]ne of ordinary skill in the art would contemplate that other analogs of ‘human growth hormone’ would also be included as well as SEQ ID NO:8” (instant response at paragraph bridging pp. 5-6).

Applicant’s remarks are acknowledged. The specification at p. 12, lines 28-31 states, “[w]hile illustrative examples of the *analog*s contemplated by the present invention are given hereinafter for G-CSF, parathyroid hormone and human growth

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hormone releasing hormone, the following teachings apply to any other biologically active proteins or polypeptides that contain substitutable residues” (emphasis added). First, contrary to applicant’s remark, it is noted that the specification indicates that SEQ ID NO:8 is human growth releasing hormone (p. 13, lines 20-22) and not an analog thereof. Second, the disclosure at p. 12, lines 28-31 of the specification appears to address *analog*s of human growth hormone releasing hormone and not the intended scope of “human growth hormone releasing hormone.” In this case, the specification clearly sets forth a definition for “human growth releasing hormone” at p. 13, lines 20-22 as follows: “[h]uman growth hormone releasing hormone (h-GHRH) is a 44 amino acid polypeptide containing glutamine residues at positions 16, 24, 30, 31 and 36 (SEQ ID NO:8).” Thus, one of ordinary skill in the art would recognize that, while *analog*s of h-GHRH may have sequences that differ from SEQ ID NO:8, one of ordinary skill in the art would recognize that h-GHRH is that which is set forth in the specification at p. 13, lines 20-22. The examiner has interpreted the term “human growth hormone releasing hormone” as recited in claims 26 and 28 accordingly.

Claim Rejections - Double Patenting

[14] The provisional obviousness-type double patenting rejection of claims 1-2, 4, 17-18, and 25-27 is withdrawn in view of the amendment to the claims and applicant’s submission of a terminal disclaimer.

Conclusion

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[15] Status of the claims:

- Claims 1, 4-24, and 26-28 are pending.
- Claims 5-16 and 19-24 are withdrawn from consideration.
- Claims 1, 4, 17-18, 26, and 28 are rejected.
- Claim 27 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.
- No claim is in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Steadman whose telephone number is 571-272-0942. The examiner can normally be reached on Monday to Friday, 7:30 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


David J. Steadman, Ph.D.
Primary Examiner
Art Unit 1656